Optimal Sedation During Severe Acute Respiratory Distress Syndrome

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KEYWORDS

• Acute respiratory distress syndrome • Analgesia • Mechanical ventilation • Sedation

KEY POINTS

- Mechanical ventilation is crucial in ARDS management but requires adequate analgesia and sedation to ensure patient comfort and proper ventilation management.
- Studies evaluating ligth sedation strategies have generally excluded patients with severe ARDS.
- Guidelines recommend minimal sedation strategies, with neuromuscular blockade reserved only for specific and severe cases.
- Identifying and treating causes of high respiratory drive, adjusting ventilation to patient needs, and only then increasing sedative doses is essential for proper management.
- Judicious opioid use and preference for non-benzodiazepine sedatives like propofol or dexmedetomidine reduce ICU stay, delirium, and mechanical ventilation duration significantly.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening condition occurring in approximately 10% to 15% of patients admitted to intensive care units (ICUs) and up to 23% of those requiring mechanical ventilation.[1] Mortality rates vary accordingly with disease severity and individualized interventions can be necessary.[1] About 25% of ARDS cases are initially classified as mild ($200 > Pao_2/Fio_2 \leq 300$ mm Hg), while the remaining 75% are moderate ($100 > Pao_2/Fio_2 \leq 200$ mm Hg) or severe

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Abbreviations	
ARDS	acute respiratory distress syndrome
ICU	intensive care unit
PADIS	pain, agitation/sedation, delirium, immobility, and sleep disruption
RASS	Richmond Agitation-Sedation Scale

(Pao_2/Fio_2 < 100 mm Hg). Moreover, one-third of mild ARDS cases progress to moderate or severe disease.[2] The LUNG-SAFE study reported hospital mortality rates of 34.9% for mild, 40% for moderate, and 46.1% for severe ARDS.[3]

Mechanical ventilation is the cornerstone in managing ARDS since it improves gas exchange and reduces the lung workload. However, mechanical ventilation can lead to ventilator-induced lung injury (VILI). To mitigate this, evidence-based guidelines recommend strategies that limit tidal volume (4–8 mL/kg predicted body weight) and inspiratory pressures (plateau pressure <30 cm H_2O).[4,5]

Analgesia and sedation are crucial in managing mechanically ventilated ARDS patients, offering several benefits such as reducing discomfort and pain, improving tolerance to mechanical ventilation, and minimizing patient-ventilator asynchrony.[1] Patient-ventilator asynchrony contributes to lung and muscle injury and reduces adherence to low tidal volume ventilation strategies.[6,7] Asynchrony incidence ranges from 10% to 85%, depending on the severity of the illness, the level of spontaneous breathing, and the degree of ventilation mismatch.[8]

However, to increase adherence to protective ventilation strategies, clinicians may end up inappropriately subjecting patients with ARDS to deep sedation for long periods. To achieve the best balance between depth of sedation and protective mechanical ventilation strategies, it is necessary to understand the role of sedation strategies, respiratory drive, and spontaneous ventilation in ARDS.

CURRENT SEDATION STRATEGIES IN ACUTE RESPIRATORY DISTRESS SYNDROME PATIENTS

Clinical guidelines, such as the Society of Critical Care Medicine's Pain, Agitation/sedation, Delirium, Immobility, and Sleep disruption1234567890-/*UIOP[]\ guidelines,[9] emphasize the importance of early rehabilitation and timely liberation from mechanical ventilation to improve outcomes. These guidelines recommend the use of short-acting sedatives (propofol or dexmedetomidine) over benzodiazepines and the adoption of a multimodal, patient-centered approach to symptom control.[10,11] Key strategies, such as daily sedation interruption, targeted light sedation, or even no sedation, are also advised, with no definitive evidence favoring one approach over the others.[9]

In patients with severe ARDS, however, deep sedation or even the use of neuromuscular blockade may be necessary, particularly during the initial phase of mechanical ventilation.[12,13] This is often due to severe dyspnea, high respiratory drive, acidosis, frequent patient-ventilator asynchrony, or severe hypoxemia necessitating prone positioning or extracorporeal membrane oxygenation.[14,15] Neuromuscular blockade improves oxygenation through several mechanisms, including reducing oxygen consumption, eliminating ventilator asynchrony, and improving thoracopulmonary compliance.[16]

The double-blind ACURASYS trial found a mortality benefit with 48 hours of neuromuscular blockade using cisatracurium in patients with moderate-to-severe ARDS (Pao_2/Fio_2 <150).[17] However, this benefit was not replicated in the larger multicenter ROSE trial,[18] which included light sedation as part of the control strategy. Notably,

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patients already receiving neuromuscular blockade at enrollment were excluded from the ROSE trial, leaving the possibility that a subset of patients could still benefit from neuromuscular blockade based on clinical judgment. Additionally, unlike the ACURASYS trial, the control group in the ROSE trial received less sedation than the neuromuscular blockade group, a factor previously associated with better ICU outcomes. While neuromuscular blockade has been shown to improve oxygenation, the need for heavy sedation during neuromuscular blockade might offset other benefits so its overall impact on mortality remains uncertain.[19]

ENROLLMENT OF PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN CLINICAL STUDIES OF SEDATION

Few trials investigating sedation management in the ICU have specifically limited enrollment to patients with ARDS.[20] Despite deep sedation remaining frequent in general ICU patients during the first 48 hours,[21] studies evaluating minimal, or no sedation strategies have generally excluded patients with severe ARDS. Regrettably, only a limited number of studies have included patients in the early phase of ARDS[22–28] (**Table 1**).

The sedation protocols used in these trials face significant challenges when applied to patients with severe ARDS, where it is often necessary to deviate from the protocol due to factors such as critically low Pao_2/Fio_2 ratio, extended periods in the prone position, or the need to escalate from light to deep sedation. Sedation must be carefully balanced depending on the severity of illness, comorbidities, and clinical need in ARDS patients and further studies in this specific population would be welcome.

THE ROLE OF RESPIRATORY DRIVE IN ACUTE RESPIRATORY DISTRESS SYNDROME

The respiratory center ultimately controls respiratory drive and responds to 4 sensory inputs: respiratory mechanics, chemical, inflammatory, and behavioral inputs. In ARDS, pulmonary interstitial and alveolar edema leads to decreased lung compliance and impairment of gas exchange that increase the mechanical and chemical inputs. In addition, inflammatory mediators can activate peripheral and pulmonary chemoreceptors. Finally, emotional responses, such as anxiety and fear, can also affect respiratory drive in ARDS patients.[29]

Assessing the respiratory drive at the bedside is essential in patients with ARDS. It can be done by observing the patient's breathing patterns, including the frequency, depth, and regularity of the breaths. One common approach is to measure the negative airway pressure generated during the first 0.1 seconds of an inspiration (P0.1). This reflects the intensity of neural respiratory drive, is an automatic measurement available on some ventilators, and can be assessed using a pressure transducer connected to the airway.[30,31]

To control respiratory drive in invasive mechanically ventilated patients with ARDS, identifying and treating underlying causes of increased respiratory drive, such as metabolic acidosis, is critical. Adjustments of ventilator settings to better match patients' needs and control respiratory drive are also paramount[29] (**Table 2**).

Spontaneous breathing may offer possible benefits for ARDS patients, such as preventing diaphragm atrophy by maintaining its activity, improving oxygenation due to a better matching of ventilation and perfusion, recruitment of collapsed alveoli, and reducing the need for sedation.[32,33] However, maintaining adequate ventilatory support during spontaneous breathing can be a challenge. Vigorous spontaneous breathing efforts can lead to large tidal volumes and high transpulmonary pressures, which

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Table 1
Randomized controlled trials evaluating strategies of sedation that included patients with acute respiratory distress syndrome

AuthorYear	Study	Time from Mechanical Ventilation to Enrollment	Patients with ARDS/Total of Enrolled Patients (%)
Kress et al,[22] 2000	Daily interruption of sedation vs usual care	48h	35/128 (23%)
Girard et al,[23] 2008	Daily interruption of sedation followed by a spontaneous breathing trial vs sedation per usual care plus a daily spontaneous breathing trial	12h	166/335 (49%)[a]
Anifantanki et al,[24] 2009	Daily interruption of sedation vs usual care	48h	15/97 (15%)
Mehta et al,[25] 2012	Protocolized sedation vs protocolized sedation plus daily sedation interruption	48h	101/243 (42%)[b]
Nassar et al,[26] 2014	Daily sedative interruption vs intermittent sedation	24h	17/60 (28%)
SRFL Trial Group[27] 2018	Sedation according to algorithm vs usual sedation practice	48h	373/1174 (32%)
Olsen et al,[28] 2020	No sedation vs light sedation	24h	298/610 (49%)

[a] Sepsis and ARDS were reported together, and the exact percentage of subjects with ARDS was not reported.
[b] ARDS was not reported, but bacterial, viral, and aspiration pneumonia were reported and are counted here as ARDS.

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Table 2
Common patient-ventilator asynchronies in patients with acute respiratory distress syndrome and their management

Patient-Ventilator Asynchrony	Description	How to Address
Reverse triggering	Mechanical insufflation triggers a muscular effort, resulting in a "patient-triggered" breath	Decrease sedation level or add a neuromuscular blocking agent
Cycling asynchronies	Premature or delayed cycling from the inspiratory to expiratory phase	Increase inspiratory time, increase tidal volume, or decrease flow
Flow asynchronies	Patient flow demand doesn't match the ventilator flow	Increase flow or change to a PC mode
High P0.1	High patient drive or insufficient levels of support	Increase ventilatory support or adjust PEEP (in case of intrinsic PEEP)

Abbreviations: PC mode, Pressure-controlled ventilation mode. PEEP, Positive end-expiratory pressure. P0.1, pressure generated during the first 0.1 s of an inspiration.

consequently exacerbate lung injury. In addition, if a patient's respiratory muscles are overloaded due to excessive effort, they can become fatigued, leading to worsening respiratory failure.[33] A recent randomized controlled trial compared pressure-controlled plus spontaneous ventilation versus volume-controlled ventilation in 700 patients with moderate and severe ARDS 24 hours after the study enrollment. Patients in the pressure-controlled plus spontaneous ventilation group received significantly less sedation than patients in the volume-controlled group. Additionally, the study did not find evidence of harm, such as a higher occurrence of pneumothorax, refractory hypoxemia, or higher mortality, in patients with spontaneous ventilation. Indeed, patients who could spontaneously ventilate required less adjunctive therapy for hypoxemia. Thus, spontaneous breathing seems safe and may even be beneficial in patients with moderate and severe ARDS.[34] Continuous bedside monitoring of respiratory parameters is pivotal in patients with ARDS ventilated in assist-control and pressure-support ventilation.

ANALGESIA, SEDATION, AND RESPIRATORY DRIVE IN ACUTE RESPIRATORY DISTRESS SYNDROME

Opioids and sedatives are commonly given to mechanically ventilated patients, but their real effect on respiratory drive in these patients is uncertain. Opioids can suppress respiratory drive by interacting with brainstem neurons or suppressing peripheral or central chemoreceptors. Despite being widely used in mechanically ventilated patients, few studies have evaluated the effects of opioids on respiratory drive. Only 2 studies in a recent systematic review suggested opioids cause a small reduction in P0.1 in mechanically ventilated patients.[35] Two other studies not included in the meta-analysis suggested that opioids such as fentanyl[36] and remifentanil[37] at doses used during mechanical ventilation do not reduce respiratory drive. However, a Spanish multicenter observational study found opioids are associated with reduced double cycling, an asynchrony that causes large tidal volumes. Furthermore, patients treated with opioids alone had the same rates of double cycling as patients treated with a combination of sedatives and opioids but were more alert.[38] Therefore,

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although opioids do not seem to reduce respiratory drive specifically, they could help reduce VILI in ARDS patients.

Benzodiazepines can depress central respiratory drive in a dose-dependent manner. However, an extensive systematic review of the effect of sedatives on the breathing pattern of mechanically ventilated patients found no study that evaluated the effect of benzodiazepines on breathing in these patients.[35] Considering that benzodiazepines are associated with many adverse effects in critically ill patients and can prolong the duration of mechanical ventilation when compared to other sedatives,[39] the use of benzodiazepines to suppress respiratory drive may not be the ideal approach for most patients.

Propofol also depresses central respiratory drive. In a study of 30 patients breathing spontaneously and receiving mechanical ventilation, Dianti and colleagues showed that when propofol was infused at lower doses ($\pm$ 25 mcg/kg/min), small increases in its infusion rate (of 10 mcg/kg/min each) reduced P0.1 and transpulmonary pressure. However, at higher doses ($\pm$ 75 mcg/kg/min), increasing inspiratory pressure did not reduce respiratory drive and even increased pulmonary distension pressure.[36] Therefore, low infusion doses of propofol can be used to modulate respiratory drive in ARDS patients ventilated in assisted modes.

Dexmedetomidine does not modify the respiratory rate and gas exchange in ICU patients. The main use of dexmedetomidine in impulse modulation in ARDS patients would be to control behavioral factors such as anxiety and agitation.[35,40]

In addition to the fact that sedatives have little or no effect on respiratory drive, deep sedation strategies also do not reduce respiratory drive. Dzierba and colleagues studied the association between respiratory drive and depth of sedation in 56 patients who required mechanical ventilation for up to 36 hours, 48 (86%) of whom were intubated due to acute respiratory failure. There was no correlation between the depth of sedation, assessed by the Richmond Agitation-Sedation Scale (RASS), and respiratory drive, measured by P0.1. Notably, 18 of the 20 highest P0.1 values, covering all 10 of the highest P0.1 values, occurred in patients who were deeply sedated (ie, RASS -3 to -5).[41] Spinelli and colleagues studied 217 mechanically ventilated patients with P0.1 measurements. They also found no association between the level of sedation measured by RASS and P0.1.[42]

Therefore, focusing solely on sedatives, opioids, and deep sedation protocols to manage respiratory drive during ARDS may not be the most effective approach. Instead, the best strategy for controlling increased respiratory drive in patients with ARDS is to identify the cause of the increased respiratory drive and treating it, adjust ventilatory parameters according to the patient's needs, and only use drugs that can help maintain a protective ventilatory strategy.

CHOICE OF OPIOIDS AND SEDATIVES IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME

Whenever possible, a light level of sedation should be targeted in mechanically ventilated patients with ARDS. However, many patients remain at deeper levels of sedation during the early phase of severe ARDS, especially those requiring neuromuscular blockers. For most of these patients, a combination of opioids and sedatives will be the rule during the early phase of mechanical ventilation.

Pain assessment is of paramount importance in mechanically ventilated patients. Pain should be assessed using validated tools, such as the behavioral pain scale[43] or the critical care pain observation tool.[44] Opioids should be administered to control pain, and if neuromuscular blockade is required, pain relief must be achieved before

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initiating the neuromuscular blocker infusion. Among the most used opioids, fentanyl has some advantages over morphine, including a faster onset and shorter duration of action, as well as fewer side effects. A study comparing fentanyl and morphine in mechanically ventilated patients found that fentanyl significantly increased the median number of ventilator-free days at day 28 compared to morphine.[45]

After pain control, sedatives can be used to provide comfort and safety. When neuromuscular blockade is not considered, sedatives can be titrated to keep patients readily awake, calm, and cooperative (ie, Richmond Agitation-Sedation Scale [RASS][46] of −2 to 0), once patients do not have frequent asynchronies with the ventilator and a protective ventilatory strategy has been achieved. In the cases where neuromuscular blockade is necessary, deeper levels of sedation (ie, RASS -4/-5) should be achieved before the start of neuromuscular blockade.

When choosing a sedative drug, nonbenzodiazepines should be preferred whenever possible. A systematic review and meta-analysis found that nonbenzodiazepine sedation strategies were associated with shorter duration of mechanical ventilation and shorter ICU length of stay compared to benzodiazepine-based regimens.[47] Furthermore, higher doses and prolonged use of benzodiazepines are linked to an increased risk of delirium compared to nonbenzodiazepine sedatives.[48]

Among nonbenzodiazepine sedatives, propofol seems to be the most suitable choice due to its effect on the modulation of respiratory drive and shorter duration of action, both of which are associated with faster extubation times compared to benzodiazepines.[49] While dexmedetomidine is also associated with a shorter duration of mechanical ventilation when compared to benzodiazepines,[47] it does not interfere with the respiratory drive and is equivalent to propofol in terms of time to extubation.[50] Thus, if adequate levels of sedation cannot be achieved with doses of propofol up to 4 mg/kg/h (approximately 65 mcg/kg/min), adding dexmedetomidine could be considered to reduce propofol cumulative dose, though the effectiveness of combining dexmedetomidine with propofol has not been studied in randomized trials. In selected cases, consider using midazolam in low doses (0.02–0.1 mg/kg/h) and for as shortest time possible to achieve target levels of sedation[12,39] (**Fig. 1**).

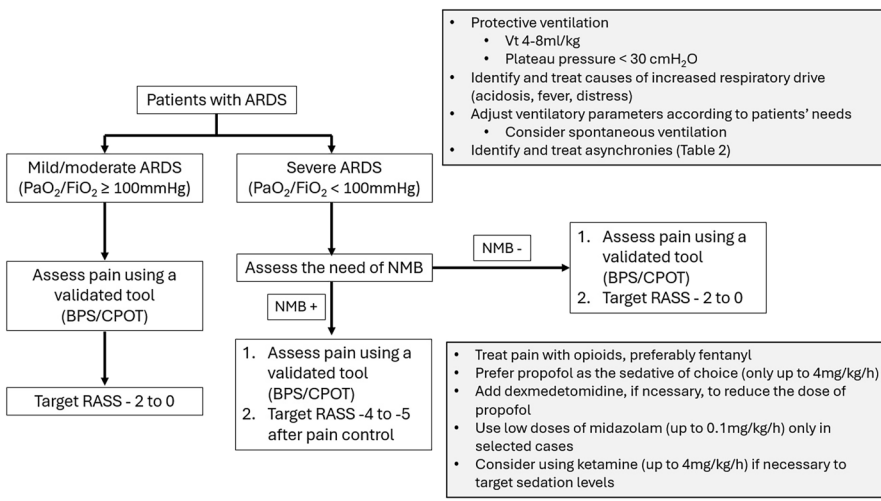
Patients with ARDS
Mild/moderate ARDS (PaO_2/FiO_2 ≥ 100mmHg)
Severe ARDS (PaO_2/FiO_2 < 100mmHg)
Assess pain using a validated tool (BPS/CPOT)
Target RASS - 2 to 0
Assess the need of NMB
NMB -
NMB +
1. Assess pain using a validated tool (BPS/CPOT)
2. Target RASS - 2 to 0
1. Assess pain using a validated tool (BPS/CPOT)
2. Target RASS -4 to -5 after pain control
• Protective ventilation
• Vt 4-8ml/kg
• Plateau pressure < 30 cmH_2O
• Identify and treat causes of increased respiratory drive (acidosis, fever, distress)
• Adjust ventilatory parameters according to patients' needs
• Consider spontaneous ventilation
• Identify and treat asynchronies (Table 2)
• Treat pain with opioids, preferably fentanyl
• Prefer propofol as the sedative of choice (only up to 4mg/kg/h)
• Add dexmedetomidine, if ncessary, to reduce the dose of propofol
• Use low doses of midazolam (up to 0.1mg/kg/h) only in selected cases
• Consider using ketamine (up to 4mg/kg/h) if necessary to target sedation levels

Fig. 1. Analgesia and sedation in mechanically-ventilated patients with ARDS. *Abbreviations*: BPS, behavioral pain scale; CPOT, critical care pain observation tool; NMB, neuromuscular blockade; Vt, tidal volume.

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Ketamine, a noncompetitive NMDA receptor antagonist, can also be an option to spare benzodiazepines, used at a dose range of 0.5 to 4 mg/kg/hr. Despite the limited literature, the retrospective KISS study suggested that ketamine use is safe and associated with reduced mortality in patients with severe ARDS.[51]

SUMMARY

Analgesia and sedation are essential components in the management of patients with ARDS, offering significant benefits such as relieving discomfort and pain, improving tolerance to mechanical ventilation, and minimizing patient-ventilator asynchrony. The complex relationship between the depth of sedation, respiratory drive, and patient-ventilator synchrony highlights the importance of individualized approaches. While light sedation is associated with better patient outcomes and fewer complications on average, patients with severe ARDS may necessitate deeper sedation targets and the administration of neuromuscular blockade, especially during the acute phase. Current evidence favors the use of nonbenzodiazepine sedatives, such as propofol or dexmedetomidine, due to their proven effectiveness in reducing ICU length of stay and dependency on mechanical ventilation in comparison to benzodiazepines.

CLINICS CARE POINTS

- In ARDS, controlling respiratory drive and monitoring spontaneous breathing are essential to optimize ventilation, minimize lung injury, and improve clinical outcomes.
- The effect of opioids on reducing respiratory drive in mechanically ventilated patients is uncertain, but these drugs appear to reduce double cycling and therefore help reduce VILI in patients with ARDS.
- Propofol reduces the respiratory drive and seems to be the best choice as a sedative for ARDS patients. However, at high doses (+/- 75 mcg/kg/min), propofol does not reduce respiratory drive and may even increase pulmonary distension pressure.
- Dexmedetomidine does not modify the respiratory rate and gas exchange in ICU patients, but may be used to control anxiety and agitation.
- Since there is no correlation between the depth of sedation and respiratory drive, intensivists should identify and treat the cause of increased respiratory drive, adjust ventilatory parameters according to patient needs, and use only drugs that can help maintain a protective ventilatory strategy.

DISCLOSURE

The authors do not have any conflicts of interest to disclose.

REFERENCES

1. Grasselli G, Tonetti T, Protti A, et al. Pathophysiology of COVID-19-associated acute respiratory distress syndrome: a multicentre prospective observational study. Lancet Respir Med 2020;8(12):1201–8.
2. Diamond M, Peniston HL, Sanghavi DK, Mahapatra S. Acute respiratory distress syndrome. 2024. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.

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3. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 2016;315(8):788–800.
4. Qadir N, Sahetya S, Munshi L, et al. An update on management of adult patients with acute respiratory distress syndrome: an official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2024;209(1):24–36.
5. Grasselli G, Calfee CS, Camporota L, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med 2023;49(7):727–59.
6. Schmidt GA, Girard TD, Kress JP, et al. Liberation from mechanical ventilation in critically ill adults: executive summary of an official American college of chest physicians/american thoracic society clinical practice guideline. Chest 2017; 151(1):160–5.
7. Thille AW, Rodriguez P, Cabello B, et al. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med 2006;32(10):1515–22.
8. de Wit M, Pedram S, Best AM, et al. Observational study of patient-ventilator asynchrony and relationship to sedation level. J Crit Care 2009;24(1):74–80.
9. Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018;46(9):e825–73.
10. Cezar AG, Castanhel FD, Grosseman S. Needs of family members of patients in intensive care and their perception of medical communication. Crit Care Sci 2023;35(1):73–83.
11. Schneider D, Rosa RG, Santos R, et al. Effects of participation in interdisciplinary rounds in the intensive care unit on family satisfaction: a cross-sectional study. Crit Care Sci 2023;35(2):203–8.
12. Chanques G, Constantin JM, Devlin JW, et al. Analgesia and sedation in patients with ARDS. Intensive Care Med 2020;46(12):2342–56.
13. Alhazzani W, Belley-Cote E, Møller MH, et al. Neuromuscular blockade in patients with ARDS: a rapid practice guideline. Intensive Care Med 2020;46(11):1977–86.
14. Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368(23):2159–68.
15. Goligher EC, Tomlinson G, Hajage D, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome and posterior probability of mortality benefit in a post hoc bayesian analysis of a randomized clinical trial. JAMA 2018;320(21):2251–9.
16. Iavarone IG, Al-Husinat L, Vélez-Páez JL, et al. Management of neuromuscular blocking agents in critically ill patients with lung diseases. J Clin Med 2024; 13(4). https://doi.org/10.3390/jcm13041182.
17. Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010;363(12):1107–16.
18. Moss M, Huang DT, Brower RG, et al. Early neuromuscular blockade in the acute respiratory distress syndrome. N Engl J Med 2019;380(21):1997–2008.
19. Ho ATN, Patolia S, Guervilly C. Neuromuscular blockade in acute respiratory distress syndrome: a systematic review and meta-analysis of randomized controlled trials. J Int Care 2020;8:12.
20. Shah FA, Girard TD, Yende S. Limiting sedation for patients with acute respiratory distress syndrome - time to wake up. Curr Opin Crit Care 2017;23(1):45–51.
21. Shehabi Y, Bellomo R, Kadiman S, et al. Sedation intensity in the first 48 hours of mechanical ventilation and 180-day mortality: a multinational prospective longitudinal cohort study. Crit Care Med 2018;46(6):850–9.

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22. Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000; 342(20):1471–7.
23. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126–34.
24. Anifantaki S, Prinianakis G, Vitsaksaki E, et al. Daily interruption of sedative infusions in an adult medical-surgical intensive care unit: randomized controlled trial. J Adv Nurs 2009;65(5):1054–60.
25. Mehta S, Burry L, Cook D, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. JAMA 2012;308(19):1985–92.
26. Nassar Junior AP, Park M. Daily sedative interruption versus intermittent sedation in mechanically ventilated critically ill patients: a randomized trial. Ann Intensive Care 2014;4:14.
27. SRLF Trial Group. Impact of oversedation prevention in ventilated critically ill patients: a randomized trial-the AWARE study. Ann Intensive Care 2018;8(1):93. https://doi.org/10.1186/s13613-018-0425-3.
28. Olsen HT, Nedergaard HK, Strøm T, et al. Nonsedation or light sedation in critically ill, mechanically ventilated patients. N Engl J Med 2020;382(12):1103–11.
29. Spinelli E, Mauri T, Beitler JR, et al. Respiratory drive in the acute respiratory distress syndrome: pathophysiology, monitoring, and therapeutic interventions. Intensive Care Med 2020;46(4):606–18.
30. Sassoon CS, Younes M. Airway occlusion pressure revisited. Am J Respir Crit Care Med 2020;201(9):1027–8.
31. Telias I, Junhasavasdikul D, Rittayamai N, et al. Airway occlusion pressure as an estimate of respiratory drive and inspiratory effort during assisted ventilation. Am J Respir Crit Care Med 2020;201(9):1086–98.
32. van Haren F, Pham T, Brochard L, et al. Spontaneous breathing in early acute respiratory distress syndrome: insights from the large observational study to understand the global impact of severe acute respiratory failure study. Crit Care Med 2019;47(2):229–38.
33. Aslam TN, Klitgaard TL, Hofsø K, et al. Spontaneous versus controlled mechanical ventilation in patients with acute respiratory distress syndrome. Current Anesthesiol Reports 2021;11(2):85–91.
34. Richard J-CM, Beloncle FM, Béduneau G, et al. Pressure control plus spontaneous ventilation versus volume assist-control ventilation in acute respiratory distress syndrome. A randomised clinical trial. Intensive Care Med 2024. https://doi.org/10.1007/s00134-024-07612-3.
35. Quickfall D, Sklar MC, Tomlinson G, et al. The influence of drugs used for sedation during mechanical ventilation on respiratory pattern during unassisted breathing and assisted mechanical ventilation: a physiological systematic review and meta-analysis. eClinicalMedicine 2024;68:102417. https://doi.org/10.1016/j.eclinm.2023.102417.
36. Dianti J, Morris IS, Bassi TG, et al. Sedation-ventilation interaction in acute hypoxemic respiratory failure: secondary analysis of the land and diaphragm-protective ventilation by means of assessing respiratory work (LANDMARK) trial. CHEST Critical Care 2024;2(2). https://doi.org/10.1016/j.chstcc.2024.100067.

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37. Costa R, Navalesi P, Cammarota G, et al. Remifentanil effects on respiratory drive and timing during pressure support ventilation and neurally adjusted ventilatory assist. Respir Physiol Neurobiol 2017;244:10–6.
38. de Haro C, Magrans R, López-Aguilar J, et al. Effects of sedatives and opioids on trigger and cycling asynchronies throughout mechanical ventilation: an observational study in a large dataset from critically ill patients. Crit Care 2019;23(1):245.
39. Carini FC, Luz M, Gusmao-Flores D. Enhancing patient care: updated sedative choices in the intensive care unit. Crit Care Sci 2024;36:e20240152en. https://doi.org/10.62675/2965-2774.20240152-en.
40. Conti G, Ranieri VM, Costa R, et al. Effects of dexmedetomidine and propofol on patient-ventilator interaction in difficult-to-wean, mechanically ventilated patients: a prospective, open-label, randomised, multicentre study. Crit Care 2016;20(1):206.
41. Dzierba AL, Khalil AM, Derry KL, et al. Discordance between respiratory drive and sedation depth in critically ill patients receiving mechanical ventilation. Crit Care Med 2021;49(12):2090–101.
42. Spinelli E, Pesenti A, Slobod D, et al. Clinical risk factors for increased respiratory drive in intubated hypoxemic patients. Crit Care 2023;27(1):138.
43. Payen JF, Bru O, Bosson JL, et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. Crit Care Med 2001;29(12):2258–63.
44. Gélinas C, Fillion L, Puntillo KA, et al. Validation of the critical-care pain observation tool in adult patients. Am J Crit Care 2006;15(4):420–7.
45. Casamento AJ, Serpa Neto A, Young M, et al. A phase II cluster-crossover randomized trial of fentanyl versus morphine for analgosedation in mechanically ventilated patients. Am J Respir Crit Care Med 2021;204(11):1286–94.
46. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond agitation-sedation scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 2002;166(10):1338–44.
47. Fraser GL, Devlin JW, Worby CP, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. Crit Care Med 2013;41(9 Suppl 1):S30–8.
48. Serafim RB, Paulino MC, Sharshar T, et al. Delirium severity in the intensive care unit. Crit Care Sci 2024;36:e20240139en. https://doi.org/10.62675/2965-2774.20240139-en.
49. Garcia R, Salluh JIF, Andrade TR, et al. A systematic review and meta-analysis of propofol versus midazolam sedation in adult intensive care (ICU) patients. J Crit Care 2021;64:91–9.
50. Heybati K, Zhou F, Ali S, et al. Outcomes of dexmedetomidine versus propofol sedation in critically ill adults requiring mechanical ventilation: a systematic review and meta-analysis of randomised controlled trials. Br J Anaesth 2022;129(4):515–26.
51. Pata R, Sandeep P, Aung HM, et al. Ketamine infusion as a sedative-analgesic in severe ARDS (KISS). J Community Hosp Intern Med Perspect 2021;11(5):619–23.

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